

Aortic dissection in Turner's syndrome: a "perfect storm"?

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THE INNOVATIVE PEDIATRIC CARDIOLOGIST, William F. Friedman, who sadly died recently,¹ would have been gratified to read the article "Clinical and epidemiological description of aortic dissection in Turner's Syndrome" by Gravholt et al.,² which appears in the current issue of the *Journal*. Gravholt et al. describe 18 cases of aortic dissection in young Swedish and Danish women with Turner's Syndrome. It was Friedman along with a colleague, Barbara Lippe, who in the early 1980s convinced a fellow in pediatric cardiology to follow-up on some intriguing case reports. The subsequent study of Lin et al.³ conclusively demonstrated that girls and young women with Turner's syndrome had a propensity for dilation of the aortic root, and that, among those individuals, a few developed severe aneurysms and catastrophic aortic dissection. Our own unpublished review of the literature has identified 84 cases of aortic dissection in patients with Turner's syndrome reported since 1964. About half of those affected were under the age of 30, and the same number died as a result of the dissection. More than 20 years after the report from Lin et al., we still know precious little about the cause of this terrible affliction, or about the risk factors that should alert clinicians to its occurrence in this vulnerable group. Furthermore, nobody is certain exactly how individuals with the syndrome should be monitored, particularly those without obvious risk factors.

A recent study by Ostberg et al.⁴ has identified an associated vasculopathy that involves intimal and medial thickening of large arteries, and dilation of the

aortic root, that is independent of the congenital cardiac malformations that commonly occur in Turner's syndrome. This data perhaps makes the recommendation of routine screening for all those with the syndrome less controversial, regardless of the presence of known risk factors. We know that hypertension, a bifoliate aortic valve, and aortic coarctation significantly increase the risk for aneurysm and dissection of the aorta in general.⁵ And there is good evidence that a bifoliate aortic valve causes aortic root dilation regardless of the degree of stenosis or regurgitation.⁶ The eminent cardiac pathologist, Jesse Edwards, pointed out that "dissecting aneurysm of the aorta may be viewed as a complication of disproportion between the strength to the aorta, on one hand, and intra luminal pressure, on the other".⁷ So it would seem that, in patients with Turner's syndrome, there is a kind of "perfect storm" of risk factors that include an hypertensive tendency, a high incidence of the bifoliate aortic valve and coarctation, and possibly an inherent weakness of the aortic wall. Unfortunately, as yet there is no direct evidence for this last factor.

The 18 cases collected by Gravholt et al.² represent the largest collection of directly-ascertained cases of aortic dissection to date, and for this they are to be congratulated. The Danish cohort provides a valuable population-based estimate. Their group is fortunate to practice medicine in a country where public health is taken seriously, and investigators can readily gain access to state-run databases. Others have collected individual reports, and compiled more cases, but these studies, and also those of Gravholt et al., are limited because they are retrospective in nature, and lack critical information. For example, in the report from Gravholt et al., the cardiac problems in three patients (#3,7,11) were insufficiently described to determine if

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they were truly risk factors. In four additional cases (#10,12,13,14), there was no cardiac information. In half of the cases, therefore, there were either unknown risk factors leading to dissection, or there was insufficient data. There are too many questions left unanswered: Were all medications reported? What did the aorta look like in the months preceding the dissection? Does treatment with growth hormone play a role in enlargement of the aortic root in those with Turner's syndrome? Indeed, the studies that have looked at these questions to date are either population-based, and describe only a few cases, or are surveys that lack critical data. If we are to understand the underlying pathophysiology of aortic dissection in the syndrome, a concerted prospective international effort will be required.

Clearly, we know too little about aortic dissection in the setting of Turner's syndrome. Moreover, clinicians often fail to recognize aortic dissection in the syndrome even as it is occurring. As a cardiologist on the health advisory board of the Turner Syndrome Society of the United States, I routinely hear tragic stories of women with the syndrome entering emergency rooms complaining of chest pain that is misinterpreted as a gastrointestinal, musculoskeletal or pulmonary problem, who then go on to die of the disease. Hopefully, publication of the report from Gravholt et al.² will serve to enlighten the international pediatric cardiologic and general medical communities to this serious problem. We can do more. My laboratory has established an international registry to track aortic dissection as it occurs in the setting of Turner's syndrome. Its purpose is

- to identify women with Turner's syndrome and aortic dissection
- to determine risk factors for aortic dissection, and

- to use this information to establish screening guidelines.

Enrollment can be done by an individual with Turner's syndrome who is currently under care for aortic dissection, by one of her physicians, or by a physician or family member who knew a deceased individual with Turner syndrome. To enroll, either use the online report form for dissection prepared by the registry, and available at http://www.turner-syndrome-us.org/resource/resources_detail.cfm?id=193; contact my team, by telephone at 00-1-503-494-9899 or by e-mail at <silberbm@ohsu.edu>; contact the registry directly at mail code CDRC-P, 3181 SW Sam Jackson Park Road, Oregon Health & Science University, Portland OR, 97201; or call 00-1-800-882-9996, and then press "3."

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